Supplementary Material

**Time-dependent insulin oligomer reaction pathway prior to fibril formation:
Cooling and seeding**

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Table

Table SI: Parameters obtained from the best fit of the empirical model (Eq. (2)) to the cooling data from **Fig. 3**

Δt_{cool}	k_{app}	t_{50}	t_{lag}	$A_{600,asym}$
(days)	(h^{-1})	(h)	(h)	(-)
0	3.76	4	3.47	1.133
1	3.83	4.03	3.52	1.127
4	3.81	4.23	3.72	1.046
7	3.68	4.27	3.72	0.954
14	5.08	4.83	4.45	0.910
21	3.23	4.80	4.18	0.831
28	2.78	4.97	4.23	0.798

Figure Legend

Fig. S1. Plot of the A600 data according to the linearized form of the empirical model (Eq. (3)) for Δt_{cool} for 0 day ($\blacklozenge$) (no cooling, reference), 1 day ($\square$), 4 days ($\triangle$), 7 days ($\bigcirc$), 14 days ($\blacksquare$), 21 days ($\blacktriangle$), 28 days ($\bullet$). The best fits with the empirical model were respectively: $y = -5.061t + 18.16$, (R^2=0.983); $y = -4.008t + 7.983$, (R^2=0.980); $y = -3.891t + 8.669$, (R^2=0.963); $y = -2.814t + 6.584$, (R^2=0.934); $y = -2.787t + 7.864$, (R^2=0.957); $y = -3.433t + 9.686$, (R^2=0.936); $y = -2.755t + 8.354$, (R^2=0.908). With $y = \ln\left(\left(1 - A_{600}\right)/A_{600}\right)$ and t = time.

Fig. S2. Apparent rate constant, k_{app}, as a function of added insulin amount, m (mg), and derived from a best-fit of the empirical model (Eq. (2)) to the data in **Fig. 10.**
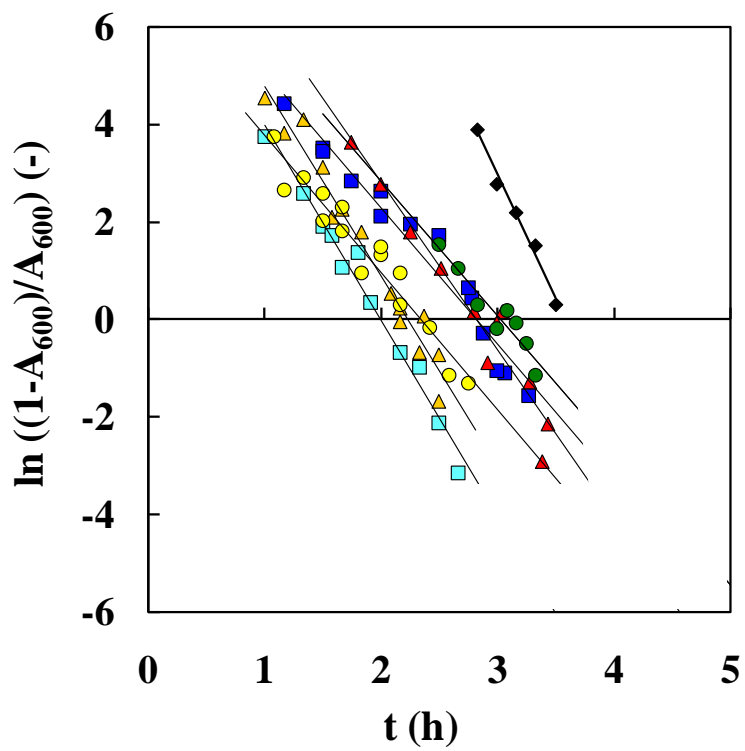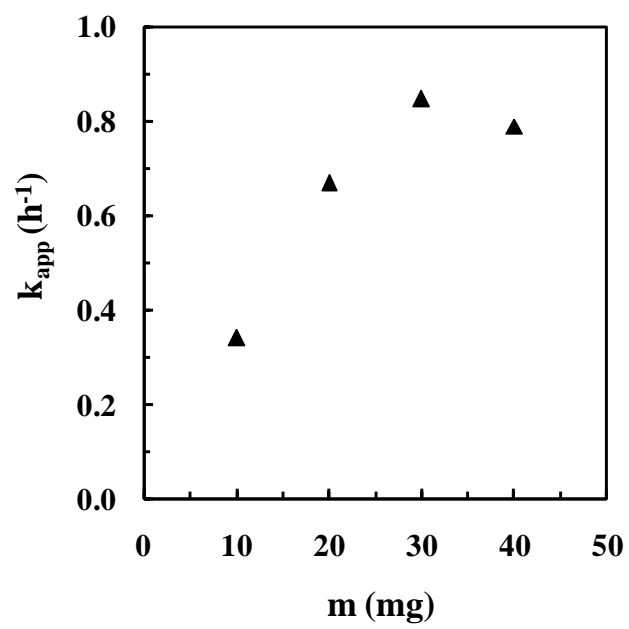
Figures

Fig. S1

Fig. S2